REMARKS

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

Claims 1, 30, 40, 57, and 73-74 are amended, while claims 80-83 are new. Support for these amendments is found in paragraphs [0015], [0056], [0088], [0101], [0104], and [0123] of the present application. No new matter has been added by way of the above amendments.

Claims 68-72 and 75-79 are cancelled. Claims 1-67, 73-74, and 80-83 are pending.

The rejection of claims 1, 30, and 40 under 35 U.S.C. § 101 as being directed to non-statutory subject matter is respectfully traversed in view of the amendments to claims 1, 30, and 40 which recite a filtration method with an explicit filtering step. Since this filtering step transforms the poly-disperse suspension to a permeate, applicants submit that the rejection under 35 U.S.C. § 101 is improper and should be withdrawn.

The rejection of claims 1-79 under 35 U.S.C. 103 (a) for obviousness over Romero et al., "Global Model of Crossflow Microfiltration Based on Hydrodynamic Particle Diffusion," *Journal of Membrane Science*, 39:157-185 (1988) ("Romero") in view of Dharmappa et al., "A Comprehensive Model for Cross-flow Filtration Incorporating Polydispersity of the Influent," *Journal of Membrane Science*, 65:173-185 (1976) ("Dharmappa") is respectfully traversed.

Romero teaches a model of crossflow microfiltration which predicts filtration flux and concentrated particle layer thickness under steady and quasi-steady operation. This model incorporates the concepts of shear-induced hydrodynamic diffusion of particles and the transport along the membrane surface of a fluid-like concentrated particle layer whose viscosity is a function of particle volume fraction.

Dharmappa teaches a semi-empirical model for prediction of foulant layer thickness and concentration to predict the permeate flux in cross-flow micro and ultrafiltration of poly-disperse influents.

The PTO asserts that the claims differ from Romero in requiring that packing densities and/or packing volume be determined for all or each of the particle sizes present. However, the PTO asserts that since Dharmappa teaches determination of particle size distributions, it would have been obvious to utilize such calculations in the manner taught by Romero to determine yield and passage multiple feed flow mixtures.

Applicants respectfully disagree. Neither Dharmappa and Romero examine particle capture, subsequent cake formation, nor transport through the formed cake.

In particular, claim 1 of the present application (and those depending from it) call for the following combination of steps: determining particle size distribution of the poly-disperse suspension; determining equivalent spherical radii of the particles; determining viscosity of the suspension; determining maximum back-transport velocity (u_i) for all particles; estimating maximum aggregate packing volume fraction (ϕ_M) for all particles at a wall of the filtration membrane from geometric considerations; selecting the particle that gives a minimum permeation flux at a given filtration membrane shear rate, wherein the selected particle has a radius (a_i); determining a predicted permeation flux (J); determining packing density ϕ_{wi} at a membrane wall for each particle size (a_j for $j \neq i$) at the predicted permeation flux; determining interstitial packing density ($\phi_{wiinterstice}$) of particles in the suspension which are the smallest; determining minimum pore diameter ($2r_{\mathrm{minimum}}$) based on the packing density of each particle; estimating yield of a target species in the filtration permeate by calculating observed sieving coefficient (S_o) for the target species, thereby predicting pressure independent permeation flux and target molecule yield in a permeate resulting from crossflow membrane filtration of particles in the poly-disperse suspension during crossflow filtration; and optimizing conditions for filtration based on the prediction of pressure independent permeation flux and target molecule yield to design a filtration system for the said poly-disperse suspension.

Claim 30 and the claims depending from it call for: providing a predicted permeation flux (J); determining packing density for all particle sizes at the predicted permeation flux; determining interstitial packing density ($\phi_{wiinterstice}$) of particles in the suspension which are smallest, thereby determining packing density at the membrane wall of particles of the poly-disperse suspension; and optimizing conditions for filtration based on the said packing density to design a filtration system for the said poly-disperse suspension.

Further, claim 40 and the claims depending from it require: determining viscosity of the suspension; determining maximum back-transport velocity (u_i) for all particles; estimating maximum aggregate packing volume fraction (ϕ_M) for all particles at a wall of the filtration membrane from geometric considerations; selecting the particle that gives a minimum permeation flux at a given filtration membrane shear rate, wherein the selected particle has a radius (a_i); determining a predicted permeation flux (J); determining packing density (ϕ_{wj}) at the membrane wall for each particle size (a_j for $j \neq i$) at the predicted permeation flux, thereby predicting pressure independent permeation flux for crossflow membrane filtration of the poly-disperse suspension; and optimizing conditions for filtration based on the prediction of permeation flux to design a filtration system for the selected poly-disperse suspension.

Finally claim 57 and the claims depending from it require: determining minimum pore diameter ($2r_{\mathrm{minimum}}$) based on the packing density of each particle; estimating yield of a target species in the filtration permeate for the poly-disperse suspension during crossflow filtration by calculating observed sieving coefficient (S_o) for the target species; and optimizing conditions for filtration based on yield of the target molecule to design a filtration system for the said poly-disperse suspension.

Neither Romero nor Dharmappa teach this combination of steps.

Romero relates permeation flux to particle layer thickness through standard filtration theory. The thickness of the particle cake is empirically related to the resistance to flow. Romero uses classical equations for mass balances and never considers individual particles. Romero fails to relate solute flow or solute retention to permeation flux and thus fails to teach the methodology of the present invention.

Dharmappa teaches a semi-empirical model for prediction of foulant layer thickness and concentration in order to predict the permeate flux in cross-flow micro and ultrafiltration of poly-disperse influents. Dharmappa teaches model parameters "a" and "b" which represent rate of change of foulant layer thickness with respect to time. These two parameters have to be estimated experimentally either by experimentally obtaining the thickness of foulant layer or by fitting observed flux. The methodology of the present invention is not semi-empirical.

Dharmappa also fails to relate dynamic particle capture and the subsequent time dependent buildup of porous cake with the prediction of transport of fluid and solute. Further, in the conclusions section, Dharmappa attributes the significant deviations between the predicted and observed flux to several factors one of which is the "negligence of actual hydraulic conditions".

For all the reasons above, the rejection of claims 1-79 for obviousness over Romero and Dharmappa is improper and should be withdrawn.

In view of all of the foregoing, applicants submit that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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